

WHAT IS CLAIMED IS:

1. A method of detecting a polymorphism site,
comprising:

5 (1) reacting a test sample containing a
polymorphism site with a plurality of types of probes
corresponding to a plurality of types of the
polymorphism site to be identified of said test sample,
said probes binding to said plurality of types of the
polymorphism site with a high affinity and being
10 labeled with marker substances so as to optically
distinguish from each other; and

(2) optically measuring and analyzing a
positional change of the marker substance at a
plurality of time points in the course of the reaction,
15 thereby detecting the types of polymorphism sites of
said test sample.

2. The method of detecting a polymorphism site
according to claim 1, wherein said marker substance is
a fluorescent substance, said detecting is performed by
20 a confocal microscope, and said analyzing is performed
by a fluorescent correlation spectroscopy.

3. The method of detecting a polymorphism site
according to claim 1, wherein the polymorphism site is
a single nucleotide polymorphism.

25 4. A method of detecting a polymorphism site,
comprising:

(1) hybridizing a test sample DNA fragment

containing a sequence of a polymorphism site with
a plurality of types of DNA probes respectively having
sequences complementary to a plurality of sequences to
be identified and contained in the test sample DNA

5 fragment, and labeled with a marker substance, said
plurality of types of probes being set so as to
optically distinguish from each other; and

(2) optically measuring and analyzing a change of
the marker substance at a plurality of time points in
10 the course of the hybridization, thereby detecting the
polymorphism site.

5. The method of detecting a polymorphism site
according to claim 4, wherein said marker substance is
a fluorescent substance, said detecting is performed by
15 a confocal microscope, and said analyzing is performed
by a fluorescent correlation spectroscopy.

6. The method of detecting a polymorphism site
according to claim 4, wherein the polymorphism site is
a single nucleotide polymorphism.

20 7. A method of detecting a polymorphism site,
comprising:

(1) hybridizing a test sample DNA fragment
containing a sequence of a polymorphism site with a
plurality of types of DNA probes respectively having
25 sequences complementary to a plurality of sequences to
be identified and contained in the test sample DNA
fragment, and having a marker-substance labeled

nucleotide corresponding to the polymorphism sites,
said plurality of types of probes being set so as to
optically distinguish from each other; and

(2) reacting a nucleic acid synthetase having a
5 repair function to a hybridized product obtained; and

(3) optically measuring and analyzing a change of
the marker substance at a plurality of time points in
the course of steps (1) and (2), thereby detecting the
polymorphism site.

10 8. The method of detecting a polymorphism site
according to claim 7, wherein said marker substance is
a fluorescent substance, said detecting is performed by
a confocal microscope, and said analyzing is performed
by a fluorescent correlation spectroscopy.

15 9. The method of detecting a polymorphism site
according to claim 7, wherein the polymorphism site is
a single nucleotide polymorphism.

20 10. The method of detecting a polymorphism site
according to claim 7, wherein said nucleic acid
synthetase is an enzyme having an exonuclease activity.

11. A method of detecting a polymorphism site,
comprising:

(1) preparing a test sample containing a
polynucleotide;

25 (2) mixing a test sample with DNA probes PR_1 to
 PR_n labeled with a detectable marker and capable of
specifically binding to polymorphism sequences PS_1 to

PS_n, thereby binding the DNA probes PR₁ to PR_n to the polynucleotide;

(3) detecting the DNA probes PR₁ to PR_n present in a micro space; and

5 (4) analyzing detection results to determine, which one of the DNA probes PR₁ to PR_n binds to the polynucleotide, thereby determining which one of the polymorphism sequences PS₁ to PS_n corresponds to a nucleotide sequence of the polymorphism site.

10 12. The method of detecting a polymorphism site according to claim 11, wherein said marker substance is a fluorescent substance, said detecting is performed by a confocal microscope, and said analyzing is performed by a fluorescent correlation spectroscopy.

15 13. The method of detecting a polymorphism site according to claim 11, wherein said polynucleotide is a gene for a human histocompatible antigen.

14. A method of detecting a polymorphism site, comprising:

20 (1) placing a test sample and a plurality of antibodies respectively having a specificity to a plurality of antigens contained in the test sample and labeled with a fluorescent substance, in a same vessel, said fluorescent substance attached to each of said
25 antibodies being set so as to be mutually distinguished; and

(2) optically measuring and analyzing

a positional change of the marker substance at a plurality of time points in the course of the reaction, thereby detecting the polymorphism site.

15 15. The method of detecting a polymorphism site according to claim 14, wherein said marker substance is a fluorescent substance, said detecting is performed by a confocal microscope, and said analyzing is performed by a fluorescent correlation spectroscopy.

10 16. The method of detecting a polymorphism site according to claim 14, wherein the polymorphism site is formed of a protein.

15 17. The method of detecting a polymorphism site according to claim 14, wherein the test sample is red blood cells and said antigen is a surface-layer antigen of red blood cells.

18. A method of detecting a polymorphism site, comprising:

20 (1) placing a test sample, a plurality of types of antigens respectively having a specificity to a plurality of antibodies to be identified contained in the test sample, and a plurality of antibodies which are the same type as said plurality of antibodies and which are labeled with a fluorescent substance, in a same vessel, the fluorescent substance labeled to each
25 of the antibodies being set so as to distinguish from each other; and

(2) optically measuring and analyzing a

19. The method of detecting a polymorphism site
5 according to claim 18, wherein said marker substance is
a fluorescent substance, said detecting is performed by
a confocal microscope, and said analyzing is performed
by a fluorescent correlation spectroscopy.

21. The method according to any one of claims 1 to 3, wherein said optical determining includes measuring fluctuation of the marker substance.

20 23. The method according to any one of claims 7 to 10, wherein said optical determining includes measuring fluctuation of the marker substance.

25 25. The method according to any one of claims 14
to 17, wherein said optical determining includes
measuring fluctuation of the marker substance.

to 20, wherein said optical determining includes measuring fluctuation of the marker substance.

0005400 43704
40227 0075000